REMARKS

Reconsideration is requested.

Claims 1-51 are pending. Claims 4, 7, 8, 12 and 17-48 have been withdrawn from consideration and canceled above, without prejudice. Claims 1-3, 5, 6, 9-11 and 13-16 will be pending upon entry of the present Amendment.

Claims 1 and 49-51 have been amended, without prejudice, to advance prosecution. Support for the amendment may be found, for example, on pages 132-138 of the specification and generally in Reference Example 1 of the specification. No new matter has been added.

The Examiner's indication that claims 11 and 13-15 contain allowable subject matter is acknowledged, with appreciation. See page 4 of the Office Action dated May 13, 2008. Claims 11, 13 and 15 have been rewritten in independent form.

To the extent not obviated by the above, the Section 103 rejection of claims 1-3, 5-6, 9-10, 16 and 49-51 over Baird (U.S. Patent No. 6,037,329), Hanai (U.S. Patent No. 5,952,472) and Owen (Journal of Immunological Methods, 1994, 168:149-165) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The cited art fails to teach or suggest the claimed method. Specifically, methods of the claims involving antibodies binding the N-terminal sequence of FGF-8, as claimed, are not taught or suggested by the combination of cited art.

The Examiner states as follows with regard to the primary reference:

> "It is undisputed that Baird et al. teach using an inhibitor of FGF-8 for therapeutic purpose (see, e.g. column 25 first full

> paragraph). Baird et al. also teach that members of the FGF family mediated pathological conditions such as arthritis (see, column 10, last paragraph)." See page 3 of the Office Action dated May 13, 2008.

The applicants respectfully disagree with the Examiner's statements regarding the teachings of the cited primary reference. Specifically, the applicants understand Bard et al. to teach using inhibitors at bFGF for inhibiting smooth muscle cell proliferation and angiogenesis, but not the therapeutic purpose. The applicants believe that Bard et at does not teach using inhibitors of all FGF family molecules for therapeutic purpose. The applicants note that the first full paragraph of column 25 of the patent, cited by the Examiner, includes the following:

> Particularly useful antisense nucleotides and triplex molecules are molecules that are complementary or bind to the sense strand of DNA or mRNA that encodes a protein involved in cell proliferation, such as an oncogene or growth factor, (e.g., bFGF, int-2, hst-1/K-FGF, FGF-5, hst-2/FGF-6, FGF-8). Other useful antisense oligonucleotides include those that are specific for IL-8 (see, e.g., U.S. Pat. No. 5,241,049; and PCT Applications WO 89/004836; WO 90/06321; WO 89/10962; WO 90/00563; and WO 91/08483). These nucleic acids or nucleic acids that encode antisense can be linked to bFGF for the treatment of psoriasis. Anti-sense oligonucleotides or nucleic acids encoding antisense specific for nonmuscle myosin heavy chain and/or c-myb (see, e.g, Simons et al. (1992) Circ. Res. 70:835-843; PCT Application WO 93/01286, U.S. application Ser. No. 07/723,454: LeClerc et al. (1991) J. Am. Coll. Cardiol. 17 (2 Suppl. A):105A; Ebbecke et al. (1992) Basic Res. Cardiol. 87:585-591) can be targeted by an FGF, for example to inhibit smooth muscle cell proliferation, such as occurs following angioplasty.

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The cited patent describes the therapeutic compositions of the patent as follows:

> The present invention generally provides therapeutic compositions. In one aspect, the composition has the formula: receptor-binding internalized ligand-nucleic acid binding domain-cytocide-encoding agent. The receptor-binding internalized ligand is a polypeptide reactive with a cell surface receptor, the nucleic acid binding domain binds to a nucleic acid, the cytocide-encoding agent is a nucleic acid molecule encoding a cytocide and which binds to the nucleic acid binding domain, and the composition binds to the cell surface receptor and internalizes the cytocide-encoding agent in cells bearing the receptor. In another aspect, the composition has the formula: receptor-binding internalized ligand-nucleic acid binding domain-prodrug-encoding agent. See Summary of the Invention, Column 2 of the cited patent.

Baird does not suggest a method of treating arthritis with an antibody as presently claimed. Baird is directed to the use of a composition with the formula "receptor-binding internalized ligand-nucleic acid binding domain-cytocide-encoding agent".

Baird is also believed to teach many growth factors and their fragments including FGF family as "a receptor-binding internalized ligand" which is capable of binding to a cell surface molecule and being internalized. Furthermore, Baird et al. teach an antisense nucleotide to growth factor including FGF family as one of inhibitors which conjugate with a receptor-binding internalized ligand. Therefore, the applicants believe that the cited patent teaches FGF-8 as one of the candidate receptor-binding internalized ligand and one of the candidate cytocide encoding-agent.

> Particularly useful antisense nucleotides and triplex molecules are molecules that are complementary or bind to the sense strand of DNA or mRNA that encodes a protein involved in cell proliferation, such as an oncogene or growth factor, (e.g., bFGF, int-2, hst-1/K-FGF, FGF-5, hst-2/FGF-6, FGF-8). See column 25, lines 13-18 of the cited patent.

The applicants submit that Baird et al. do not teach or suggest a specific inhibitor against FGF-8 protein and/or an effect of inhibiting FGF-8 protein. The applicants further submit that Baird et al. do not teach or suggest a monoclonal antibody against FGF-8 proteins. Expressing mRNA of FGF-8 on a tissue is not necessarily concerned with an expression of FGF-8 protein on the tissue. Even if the suppression of mRNA of FGF-8 on a tissue by using the inhibitor is disclosed, the applicants believe that an ordinarily skilled person in the art would not have reasonably predicted from the cited art that inhibiting FGF-8 protein would produce the beneficial results described in the present application.

The applicants believe that Baird et al. also teach the function of FGF family and pathological role of FGF family, for example, in tumor development, rheumatoid arthritis, proliferative diabetic retinopathies and other complications of diabetes, as noted in the following column 10, last paragraph of the patent, also cited by the Examiner.

> FGFs exhibit a mitogenic effect on a wide variety of mesenchymal, endocrine and neural cells and are also important in differentiation and development. Of particular interest is their stimulatory effect on collateral vascularization and angiogenesis. In some instances, FGF-induced mitogenic stimulation may be detrimental. For example, cell proliferation and angiogenesis are an integral aspect of tumor growth. Members of the FGF family, including bFGF, are thought to play a pathophysiological role, for example, in tumor development, rheumatoid arthritis, proliferative diabetic retinopathies and other complications of diabetes. To reduce or eliminate mitogenesis, muteins of FGF are constructed as described below. Such muteins retain the ability to bind to high and low affinity receptors.

The applicants believe however that Baird et al do not teach that FGF-8, one of the FGF family, is related to rheumatoid arthritis.

The applicants believe that one of ordinary skill in the art would not have reasonably predicted from the cited art that a specific FGF molecule of the present claims is related to specific pathological conditions of the claims. Therefore, the applicants believe that it would not have been obvious for an ordinarily skilled person in the art to have predicted a role of FGF-8 in the pathological condition of rheumatoid arthritis.

The applicants submitted that the secondary art fails to cure these deficiencies of the primary reference and that the claims would not have been obvious over the combination of the cited Bard et al., Hanai et al. and Owen.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required in this regard.

Respectfully submitted,

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